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☐	L60	L39 and (targeting)adj(HIV)adj(infected)adj(cell)same(MHC)	0
☐	L59	L57 and anti-HLA	0
☐	L58	L57 and anti-HIV	38
☐	L57	L56 and HIV	214
☐	L56	L55 and targeting	870
☐	L55	L39 and liposome	2154
☐	L54	L52 and targeting	15
☐	L53	L52 and liposome	12
☐	L52	(HLA-DR)adj(antibod?)	34
☐	L51	(HLA-DR)adj(antibod?)adj(conjugate)	0
☐	L50	(anti-HLA)adj(conjugate)same(liposome)	0
	DB=USPT; PLUR=YES; OP=OR		
☐	L49	L48 and (conjugated)adj(liposome)	73
☐	L48	L47 and liposome	97
☐	L47	L46 and MHC	98
☐	L46	L45 and HIV	309
☐	L45	L44 and targeting	410
☐	L44	L43 and antibody	477
☐	L43	L1 and coupling	485
☐	L42	L41 and HLA-DR	2
☐	L41	L39 and (targeting)adj(liposome)	166
☐	L40	L39 and anti-HLA	6
☐	L39	424/9.321,9.34,9.51,450;514/934.ccls.	3029
	DB=EPAB; PLUR=YES; OP=OR		
☐	L38	WO-9742962-A1.did.	1
	DB=DWPI; PLUR=YES; OP=OR		
☐	L37	9742962	2
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L36	L35 and HIV	8
☐	L35	L1 and diacylphosphatidylcholine	11

☐	L34	l1 and diacylphosphatidylglycerol	3
☐	L33	L32 and anti-HLA	13
☐	L32	L1 and HLA	405
☐	L31	L27 and anti-HLA	0
☐	L30	L27 and (diacylphosphosphatidyl)adj(glycerol)	0
☐	L29	L27 and (phosphosphatidyl)adj(glycerol)	0
☐	L28	L27 and phosphosphatidylglycerol	0
☐	L27	L26 and diacylphosphatidylcholine	101
☐	L26	(liposome)	81312
☐	L25	(liposome)same(diacylphosphatidylcholine)adj (diacylphosphyatidylglycerol)	0
☐	L24	L18 and DSPC	32
	DB=USPT; PLUR=YES; OP=OR		
☐	L23	5773027.pn.	1
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L22	L21 and HLA-DR	25
☐	L21	L18 and infectious	948
☐	L20	L18 and anti-HLA-DR	6
☐	L19	L18 and anti-HLA	6
☐	L18	(conjugated)adj(liposome)	2941
☐	L17	L15 and anti-HLADR	0
☐	L16	L15 and anti-HLA-DR	5
☐	L15	L1 and conjugated	3420
☐	L14	L12 and (HLA)adj(DR)	49
☐	L13	L12 and conjugated liposome	81315
☐	L12	L11 and conjugate	751
☐	L11	L10 and macrophage	816
☐	L10	L9 and CD4	1402
☐	L9	L8 and HIV	3070
☐	L8	L1 and targeting	3558
☐	L7	(HLA-DR)same(antibod?)same(conjugated)same(liposome)	0
☐	L6	(anti-HLA-DR)adj(liposome)	0
☐	L5	(anti-HLA-DR)same(liposome)	4
☐	L4	L1 and anti-HLA-DR	6
☐	L3	L2 and targeting	87
☐	L2	L1 and HLA-DR	91
☐	L1	(immunoliposomes)	3913

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=> s liposome conjugate
L1          358 LIPOSOME CONJUGATE

=> s l1 and anti-HLA-DR
L2            0 L1 AND ANTI-HLA-DR

=> s l1 and anti-HLA
L3            0 L1 AND ANTI-HLA

=> s l1 and HLA
L4            2 L1 AND HLA

=> dup remove l4
PROCESSING COMPLETED FOR L4
L5            2 DUP REMOVE L4 (0 DUPLICATES REMOVED)

=> d l5 1-2 cbib abs

L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
2006:1063108  Document No. 145:417029  Methods for generating stably linked
     complexes composed of homodimers, homotetramers or dimers of dimers.
     Chien, Hsing Chang; Goldenberg, David M.; McBride, William J.; Rossi,
     Edmund A. (Ibc Pharmaceuticals, Inc., USA).  PCT Int. Appl. WO 2006107617
     A2 20061012, 105pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ,
     BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ,
     EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
     KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,
     MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
     SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
     YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR,
     GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
     (English).  CODEN: PIXXD2.  APPLICATION: WO 2006-US10762 20060324.
     PRIORITY: US 2005-668603P 20050406; US 2005-728292P 20051019; US
     2005-751196P 20051216.
AB   The authors disclose dimerization and docking domain (DDD) sequences for
     the generation of stably tethered structures of defined compns., which may
     have multiple functionalities and/or binding specificities.  The tethered
     constructs may be virtually any mol. or structure, such as antibodies,
     antibody fragments, antibody analogs or mimetics, aptamers, binding
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peptides, fragments of binding proteins, known ligands for proteins or other mols., enzymes, detectable labels or tags, therapeutic agents, toxins, pharmaceuticals, cytokines, interleukins, interferons, radioisotopes, proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides, natural or synthetic polymeric substances, nanoparticles, quantum dots, organic or inorg. compds., etc. In one example, a fusion construct of a DDD sequence with an anti-CEA Fd fragment was prepared and shown to target colorectal cancer in a xenograft model.

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
1999:119837 Document No. 130:195756 Conjugates of polymers and antibodies specific for T lymphocytes, and their use as adjuvants. Chang, Tse Wen (Tanox Biosystems, Inc., USA). U.S. US 5872222 A 19990216, 6 pp., Cont.-in-part of U.S. Ser. No. 926.566, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-993291 19921218. PRIORITY: US 1991-688000 19910419; US 1992-819449 19920110; US 1992-926566 19920806.
AB Disclosed are conjugates including a substantially nonimmunogenic polymer backbone or microbead and binding mols., such as Fv, Fab, or F(ab')2 fragments of monoclonal antibodies or whole antibodies that are bound through their Fc carbohydrate moieties or have their Fc portion modified so that they cannot effect ADCC (antibody-dependent cellular cytotoxicity) or complement-mediated cytolysis, and that are specific for a T cell surface antigen, such as CD3, TCR, CD4, CD8, or CD28 on T cells. The polymer or microbead is preferably made of cross-linked dextran, ficoll, latex, or agarose, and is preferably of 0.1 to 10 μm in size, so that it can be suspended in fluids for in vivo applications. These conjugates can be used as adjuvants to enhance the antibody response against an administered immunogen.

=> s anti-HLA-DR conjugate
L6 0 ANTI-HLA-DR CONJUGATE

=> s conjugate?
L7 504884 CONJUGATE?

=> s l7 and HLA-DR
L8 827 L7 AND HLA-DR

=> s l8 and liposome
L9 22 L8 AND LIPOSOME

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 18 DUP REMOVE L9 (4 DUPLICATES REMOVED)

=> d l10 1-18 cbib abs

L10 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2006:1063108 Document No. 145:417029 Methods for generating stably linked complexes composed of homodimers, homotetramers or dimers of dimers. Chien, Hsing Chang; Goldenberg, David M.; McBride, William J.; Rossi, Edmund A. (Ibc Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2006107617 A2 20061012, 105pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-US10762 20060324. PRIORITY: US 2005-668603P 20050406; US 2005-728292P 20051019; US 2005-751196P 20051216.
AB The authors disclose dimerization and docking domain (DDD) sequences for

the generation of stably tethered structures of defined compns., which may have multiple functionalities and/or binding specificities. The tethered constructs may be virtually any mol. or structure, such as antibodies, antibody fragments, antibody analogs or mimetics, aptamers, binding peptides, fragments of binding proteins, known ligands for proteins or other mols., enzymes, detectable labels or tags, therapeutic agents, toxins, pharmaceuticals, cytokines, interleukins, interferons, radioisotopes, proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides, natural or synthetic polymeric substances, nanoparticles, quantum dots, organic or inorg. compds., etc. In one example, a fusion construct of a DDD sequence with an anti-CEA Fd fragment was prepared and shown to target colorectal cancer in a xenograft model.

L10 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2006:469702 Document No. 144:463824 Stem cells, method for their purification, identification, and use. Romagnani, Paola; Annunziato, Francesco; Maggi, Enrico; Romagnani, Sergio (Azienda Ospedaliera Careggi, Italy). PCT Int. Appl. WO 2006051112 A1 20060518, 20 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-EP55950 20051114. PRIORITY: IT 2004-FI238 20041115.

AB Herein is described a new population of circulating CD14+ cells, with a low d. surface expression of CD34 and endowed with stem capacity, a method for their purification and identification, and their therapeutic use.

L10 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2006:782978 Document No. 145:209253 Oligomers of MHC complexes. Schwabe, Nikolai Franz Gregor (Proimmune Limited, UK). Brit. UK Pat. Appl. GB 2422834 A 20060809, 42pp. (English). CODEN: BAXXDU. APPLICATION: GB 2005-2333 20050204.

AB The authors disclose the oligomerization of MHC-peptide complexes wherein the cognate peptide bound in the peptide-binding groove of the complex has a modification which allows specific oligomerization. In one example, the authors construct a soluble monomeric HLA-DR1 complex with an aldehyde-functionalized peptide of influenza hemagglutinin. Oligomerization to an octamer was effected by reaction of the foregoing monomer with an hydrazinopyridyl peptide dendrimer.

L10 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2006:1157887 Document No. 146:3760 Diagnostic chip, kit and method based on flow cytometer-microcarrier technique. Lin, Yuan (Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1854735 A 20061101, 31pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 2010-41973 20050419.

AB The title method comprises: (1) immobilizing different biomols., such as antigen/antibody, on microcarriers with at least one diameter, and labeling by fluorescent dyes with different intensities to form a fluorescence gradient (hereinafter referred to as autofluorescence), (2) incubating at least one kind of microcarrier-biomol. conjugate together with samples to combine the ligands to be detected, and combining the anti-ligand antibodies labeled by fluorescent dyes (hereinafter referred to as detecting fluorescence), (3) collecting in a flow cytometer, determining microcarrier sizes, and capturing microcarriers in different diameter ranges into a same tube, and (4) selecting microcarriers with different sizes, and determining the ligands through comparing the autofluorescence and the detecting fluorescence. This invention also provides the high-selectivity diagnostic kits based on flow-cytometer-microcarrier technique for diagnosing infectious diseases, allergic diseases, autoimmune diseases, transplant rejection and tumors, and measuring vaccine titers.

L10 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2005:696640 Document No. 143:199740 Onconase complex conjugated with folate for diagnosis and treatment of cancer, infection, cardiovascular disorder and autoimmune disease. Hansen, Hans J.; McBride, William J.; Goldenberg, David M.; Rossi, Edmund A.; Chang, Chien-Hsing Ken (Immunomedics, Inc., USA). PCT Int. Appl. WO 2005069994 A2 20050804, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US2193 20050124. PRIORITY: US 2004-538396P 20040122.

AB Because the folate receptor (also called the folate binding protein, FBP) is overexpressed on certain malignant cell types, targeting of the folate receptor has been proposed as a potential mechanism for delivery of drugs and/or radiopharmaceuticals to treat cancer. Onconase and/or variants with ribonucleolytic activity, such as rapLR1, present useful therapeutic mols. for preparing folate conjugates and complexes. The conjugates and complexes can be targeted to and internalized by targeted tissues. The conjugates and complexes may be formulated with a pharmaceutically acceptable excipient to form a primary therapeutic agent. The conjugates and complexes may be useful as primary therapeutic agents, which may be administered with addnl. therapeutic or diagnostic agents. Also disclosed are kits that include the conjugates and complexes.

L10 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2005:121072 Document No. 142:217385 Humanized and chimeric anti-CD19 antibodies, fragments and conjugates for diagnosis and treatment of B cell malignancies and autoimmune diseases. Hansen, Hans J.; Qu, Zhengxing; Goldenberg, David M. (Immunomedics, Inc., USA). PCT Int. Appl. WO 2005012493 A2 20050210, 81 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US24636 20040802. PRIORITY: US 2003-491282P 20030731.

AB The present invention provides humanized, chimeric and human anti-CD19 antibodies, anti-CD19 antibody fusion proteins, and fragments thereof that bind to a human B cell marker. Such antibodies, fusion proteins and fragments thereof are useful for the treatment and diagnosis of various B-cell disorders, including B-cell malignancies and autoimmune diseases.

L10 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2005:1027916 Document No. 143:324783 Artificial antigen-presenting cells comprising liposome, MHC-antigen peptide complex and costimulatory molecule for expanding antigen-specific T cells against autoimmune disease, allergy, transplant rejection, cancer and viral infection. Albani, Salvatore (USA). U.S. Pat. Appl. Publ. US 2005208120 A1 20050922, 97 pp., Cont.-in-part of U.S. Ser. No. 756,983. (English). CODEN: USXXCO. APPLICATION: US 2004-960855 20041006. PRIORITY: US 1998-105018P 19981020; US 1999-421506 19991019; WO 1999-US24666 19991019; US 2001-756983 20010109; US 2003-510645P 20031010.

AB The present invention concerns artificial antigen presenting cells (aAPCs) and methods of making and using the same, for example, to isolate, identify, and expand T cell populations specifically reactive against a disease-associated antigenic peptide, as well as to modulate responses of antigen-specific T cells both in vivo, ex vivo, and in vitro.

Accordingly, the aAPCs of the invention can be used to treat conditions that would benefit from modulation of a T cell response, for example, autoimmune disorders, allergies, cancers, viral infections, and graft rejection. In certain preferred embodiments, the aAPCs are liposomes comprised of MHC:peptide complexes and accessory mols. Other mols., such as co-stimulatory mols. and adhesion mols., can also be included in the compns. of the invention. In other embodiments, the aAPCs are comprised of a scaffold to which a plurality of MHC:peptide complexes and accessory mols. (as well as other mols.) can be attached at high d.

L10 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2005:98817 Document No. 142:183318 D-amino acid peptide conjugates in radioimmunotherapy and radiol. diagnosis. McBride, William J.; Goldenberg, David M. (Immunomedics, Inc., USA). U.S. Pat. Appl. Publ. US 2005025709 A1 20050203, 62 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-866180 20040614. PRIORITY: US 2003-478403P 20030613.

AB The present invention provides compds. of the formula X-R1-D-[Dpr, Orn or Lys](A)-R2 (Z)-D-[Dpr, Orn or Lys](B)-R3(Y)-NR4R5; or R1 (X)-D-[Dpr, Orn or Lys](A)-R2 (Z)-D-[Dpr, Orn or Lys](B)-R3(Y)-NR4R5, in which X is a hard acid cation chelator, a soft acid cation chelator or Ac-, R1, R2 and R3 are independently selected from a covalent bond or one or more D-amino acids that can be the same or different, Y is a hard acid cation chelator, a soft acid cation chelator or absent, Z is a hard acid cation chelator, a soft acid cation chelator or absent, and A and B are haptens or hard acid cation chelators and can be the same or different, and R4 and R5 are independently selected from the group consisting of hard acid cation chelators, soft acid cation chelators, enzymes, therapeutic agents, diagnostic agents and H. Multi-specific antibodies against a targetable construct are used that are capable of carrying one or more diagnostic or therapeutic agents. By using this approach the characteristics of the chelator, metal chelate complex, therapeutic agent or diagnostic agent can be varied to accommodate differing applications, without raising new multi-specific antibodies. The present invention also provides methods of using these compds. in radioimmunotherapy and radiol. diagnosis and kits containing the compds.

L10 ANSWER 9 OF 18 MEDLINE on STN DUPLICATE 1
2005149671. PubMed ID: 15781116. Effect of synthetic lipopeptides formulated in liposomes on the maturation of human dendritic cells. Espuelas Socorro; Roth Audrey; Thumann Christine; Frisch Benoit; Schuber Francis. (Laboratoire de Chimie Bioorganique, UMR 7514 CNRS-Universite Louis Pasteur, Faculte de Pharmacie, 74 route du Rhin, 67400 Strasbourg-Illkirch, France.) Molecular immunology, (2005 Apr) Vol. 42, No. 6, pp. 721-9. Journal code: 7905289. ISSN: 0161-5890. Pub. country: England: United Kingdom. Language: English.

AB Diacylated (e.g. MALP-2) and triacylated (Pam(3)Cys derivatives) lipopeptides, deriving from the N-terminal moiety of respectively mycoplasmal and E. coli lipoproteins, are powerful adjuvants recognized by Toll-like receptors (TLR) which have been used successfully to trigger cell activation and immune responses. To design liposome-based vaccination constructs in which Th and CTL epitopes are conjugated to synthetic lipopeptide analogues anchored into the bilayers of the vesicles, the peptide moieties of the lipopeptides were functionalized with thiol-reactive groups, such as maleimide (Mal) or bromoacetyl, incorporated into liposomes and reacted with thiol carrying peptide epitopes. Because dendritic cells (DCs) play a key role as antigen-presenting cells in immune responses, in the present study we have evaluated the impact of the functionalization of lipopeptide analogues Pam(2)CAG, Pam(3)CAG and Ol(3)GAG on the phenotypic maturation of human monocyte-derived DCs. The intrinsic cellular activities of the lipopeptide analogues incorporated into liposomes were monitored, in vitro, by measuring the up-regulation of the cell-surface markers CD80, CD83, CD86 and HLA-DR. We found that in some cases their functionalization with thiol-reactive groups led to a loss of activity. The stimulatory potency can be ranked in the following

order: Pam(3)CAG>/=Pam(2)CAG-Mal-Th approximately Pam(2)CAG-Mal>Pam(3)CAG-Mal-Th (where Th is a HS-peptide) and no appreciable activity was detected for Pam(3)CAG-Mal, Ol(3)CAG-Mal and Ol(3)CAG-Mal-Th. Our findings indicate that subtle modifications in the peptide moiety of lipopeptides have a great impact on the immunomodulatory properties of these molecules. For the engineering of liposome/lipopeptide-based vaccines, the maleimide derivative of Pam(2)CAG appears to be the best candidate.

L10 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2004:934484 Document No. 141:409779 Polyvalent protein complexes including trivalent bispecific chimeric antibodies and conjugates for diagnosis and treatment of cancer, infection, cardiological disorder and autoimmune disease. Rossi, Edmund A.; Chang, Chien-Hsing; McBride, William J. (IBC Pharmaceuticals, USA; Immunomedics, Inc). PCT Int. Appl. WO 2004094613 A2 20041104, 148 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US12662 20040422. PRIORITY: US 2003-464532P 20030422; US 2003-525391P 20031124.

AB The invention provides for a polyvalent protein complex (PPC) comprising two polypeptide chains generally arranged laterally to one another. Each polypeptide chain typically comprises 3 or 4 'v-regions', which comprise amino acid sequences capable of forming an antigen binding site when matched with a corresponding v-region on the opposite polypeptide chain. Up to about 6 'v-regions' can be used on each polypeptide, chain. The v-regions of each polypeptide chain are connected linearly to one another and may be connected by interspersed linking regions. When arranged in the form of the PPC, the v-regions on each polypeptide chain form individual antigen binding sites.

L10 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2004:934160 Document No. 141:388650 Anti-CD74 immunoconjugates and their therapeutic and diagnostic uses. Griffiths, Gary L.; Hansen, Hans J.; Goldenberg, David M.; Lundberg, Bo B. (Immunomedics, Inc., USA). U.S. Pat. Appl. Publ. US 2004219203 A1 20041104, 44 pp., Cont.-in-part of U.S. Ser. No. 377,122. (English). CODEN: USXXCO. APPLICATION: US 2003-706852 20031112. PRIORITY: US 2003-377122 20030303; US 2003-350096 20030124; US 2002-314330 20021209; US 2001-965796 20011001; US 2000-590284 20000609; US 1999-307816 19990510; US 2003-478830P 20030617; US 2002-360259P 20020301.

AB Disclosed are compns. that include anti-CD74 immunoconjugates and a therapeutic and/or diagnostic agent. Also disclosed are methods for preparing the immunoconjugates and using the immunoconjugates in diagnostic and therapeutic procedures. The compns. may be part of a kit for administering the anti-CD74 immunoconjugates compns. in therapeutic and/or diagnostic methods. Anti-CD74 binding mols. are conjugated to the one or more lipids by one or more of a sulfide linkage, a hydrazone linkage, a hydrazine linkage, an ester linkage, an amido linkage, an amino linkage, an imino linkage, a thiosemicarbazone linkage, a semicarbazone linkage, an oxime linkage, a carbon-carbon linkage. Anti-CD74 immunoconjugates comprise a drug, a prodrug, a toxin, an enzyme, a radioisotope, an immunomodulator, a cytokine, a hormone, an antibody., an oligonucleotide, or a photodynamic agent.

L10 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
2003:719520 Document No. 139:259964 Bispecific antibody mutants with enhanced rate of clearance for diagnosis and treatment of immune, autoimmune, cardiovascular and neurological diseases. Qu, Zhengxing; Hansen, Hans; Goldenberg, David M. (Immunomedics, Inc., USA; McCall, John Douglas). PCT Int. Appl. WO 2003074569 A2 20030912, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB871 20030303. PRIORITY: US 2002-361037P 20020301.

AB A mutant bispecific antibody that includes (a) a human hinge constant region from IgG having one or more amino acid mutations in the CH2 domain, (b) two scFvs; and (c) two Fvs has been constructed. This type of antibody displays enhanced clearance, which has been found to be particularly useful in the context of pre-targeting methods. The bispecific antibody mutants are useful for conjugated with therapeutic or diagnostic agents for diagnosis and treatment of immune disease, autoimmune disease, cardiovascular disease, neurol. disease, organ graft rejection, or graft vs. host disease.

L10 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2003:719519 Document No. 139:259963 Anti-CD74 antibodies and conjugates for diagnosis and treatment of immune and autoimmune diseases, infections and cancers. Hansen, Hans; Leung, Shui-on; Qu, Zhengxing; Goldenberg, David M. (Immunomedics, Inc., USA; McCall, John Douglas). PCT Int. Appl. WO 2003074567 A2 20030912, 91 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-GB890 20030303. PRIORITY: US 2002-360259P 20020301.

AB The present invention provides humanized, chimeric and human anti-CD74 antibodies, CD74 antibody fusion proteins, immunoconjugates, vaccines and bispecific that bind to CD74, the major histocompatibility complex (MHC) class-II invariant chain, Ii, which is useful for the treatment and diagnosis of B-cell disorders, such as B-cell malignancies, other malignancies in which the cells are reactive with CD74, and autoimmune diseases, and methods of treatment and diagnosis.

L10 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2003:836381 Document No. 139:341719 Use of bi-specific antibodies for pre-targeting diagnosis and therapy. Goldenberg, David M.; Hansen, Hans J.; Leung, Shui-on; McBride, William J.; Qu, Zhengxing (Immunomedics, Inc., USA). U.S. Pat. Appl. Publ. US 2003198595 A1 20031023, 59 pp., Cont.-in-part of U.S. Ser. No. 823,746. (English). CODEN: USXXCO. APPLICATION: US 2002-150654 20020517. PRIORITY: US 2001-823746 20010403; US 1999-382186 19990823; US 1998-104156P 19981014; US 1998-90142P 19980622; US 1999-337756 19990622.

AB The present invention relates to a bi-specific antibody or antibody fragment having at least one arm that specifically binds a targeted tissue and at least one other arm that specifically binds a targetable construct. The targetable construct comprises a carrier portion which comprises or bears at least one epitope recognizable by at least one arm of said bi-specific antibody or antibody fragment. The targetable construct further comprises one or more therapeutic or diagnostic agents or enzymes. The invention provides constructs and methods for producing the bi-specific antibodies or antibody fragments, as well as methods for using them.

L10 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2002:4988 Document No. 137:174682 Targeted delivery of indinavir to HIV-1 primary reservoirs with immunoliposomes. Gagne, Jean-Francois; Desormeaux, Andre; Perron, Sylvie; Tremblay, Michel J.; Bergeron, Michel

G. (Centre de Recherche en Infectiologie, Universite Laval, Centre Hospitalier Universitaire de Quebec, Quebec, QC, Can.). Biochimica et Biophysica Acta, Biomembranes, 1558(2), 198-210 (English) 2002. CODEN: BBBMBS. ISSN: 0005-2736. Publisher: Elsevier B.V..

AB The tissue distribution of indinavir, free or incorporated into sterically stabilized anti-HLA-DR immunoliposomes, has been evaluated after a single s.c. injection to C3H mice. Administration of free indinavir resulted in low drug levels in lymphoid organs. In contrast, sterically stabilized anti-HLA-DR immunoliposomes were very efficient in delivering high concns. of indinavir to lymphoid tissues for at least 15 days post-injection increasing by up to 126 times the drug accumulation in lymph nodes. The efficacy of free and immunoliposomal indinavir has been evaluated in vitro. Results showed that immunoliposomal indinavir was as efficient as the free agent to inhibit HIV-1 replication in cultured cells. The toxicity and immunogenicity of repeated administrations of liposomal formulations have also been investigated in rodents. No significant differences in the levels of hepatic enzymes of mice treated with free or liposomal indinavir were observed when compared to baseline and control untreated mice. Furthermore, histopathol. studies revealed no significant damage to liver and spleen when compared to the control group. Liposomes bearing Fab' fragments were 2.3-fold less immunogenic than liposomes bearing the entire IgG. Incorporation of antiviral agents into sterically stabilized immunoliposomes could represent a novel therapeutic strategy to target specifically HIV reservoirs and treat more efficiently this retroviral infection.

L10 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

2001:434842 Document No. 135:45176 HLA class I A2 tumor associated antigen peptides and vaccine compositions. Fikes, John; Sette, Alessandro; Sidney, John; Southwood, Scott; Celis, Esteban; Keogh, Elissa; Chesnut, Robert (Epimmune Inc., USA). PCT Int. Appl. WO 2001041741 A1 20010614, 86 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US34318 20001213. PRIORITY: US 1999-PV170448 19991213; US 2000-543608 20000405; US 2000-583200 20000530.

AB A plurality of peptide epitopes can be used to monitor an immune response to a tumor-associated antigen or, when two or more peptides are combined, can be used to create a cancer vaccine that stimulates the cellular arm of the immune system. In particular, the vaccines mediate immune responses against tumors in persons who have HLA-A2 mols. The peptide epitopes stimulate helper T-cell and cytotoxic T-cell responses. Altered peptides, peptide analogs, have enhanced biol. activities. The epitopes are from CEA, HER2/neu, MAGE2, MAGE3, or p53.

L10 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

1998:486512 Document No. 129:184814 A novel method of cell-specific mRNA transfection. Sawai, Keisuke; Ohno, Kouichi; Iijima, Yasushi; Levin, Brandi; Meruelo, Daniel (Department of Pathology and Kaplan Cancer Center, New York University Medical Center, New York, NY, 10016, USA). Molecular Genetics and Metabolism, 64(1), 44-51 (English) 1998. CODEN: MGMEFF. ISSN: 1096-7192. Publisher: Academic Press.

AB In this study, we developed a cell-specific mRNA transfection system using streptavidin-protein A (ST-PA) fusion protein and monoclonal antibodies (mAbs). We previously reported that ST-PA fusion protein and mAb complexes can transfer certain biotinylated proteins into specific cell types. At this time, we combined an in vitro transcribed biotinylated and self-replicating Sindbis virus genomic RNA with ST-PA fusion protein and mAbs. In the presence of cationic liposomes, to prevent RNA

degradation, this complex is able to transfect a reporter gene to specific cancer cells in a mAb dose-dependent manner. Even in the absence of cationic liposomes, biotinylated mRNA, ST-PA fusion, and mAb complexes can transfer some types of cancer cell suspension cultures. This cell-specific transfection system is a novel method of introducing various mRNAs into cells that results in high levels of transient protein expression. (c) 1998 Academic Press.

L10 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
1989:453742 Document No. 111:53742 Lymphocyte function-associated antigen 3 (LFA-3) purification by immuoaffinity column chromatography. Dustin, Michael; Springer, Timothy (Dana-Farber Cancer Institute, Inc., USA). Eur. Pat. Appl. EP 280578 A2 19880831, 8 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1988-301709 19880226. PRIORITY: US 1987-19010 19870226.
AB A method for purifying a 60,000-mol.-weight LFA-3 (I) is described. The method uses an anti-LFA-3 antibody affinity column. Methods are also described for detecting cells bearing CD2 antigen and for separating CD2 antigen-bearing cells from other cells. Monoclonal antibody (MAb) to I was prepared by standard techniques by fusing spleen cells from BALB/c mice injected with HLA-DR cytolytic T-lymphocytes (CTL) with P3X63Ag8.653 or NSI and growing hybridomas which showed >30% inhibition of killing of target cells by CTLs. Purified MAb TS2/9 was coupled to Sepharose CL-4B by a modification of the method of Mar. A human erythrocyte lysate containing I was passed through a mouse IgG-Sepharose-CL-4B column and then the anti-I affinity column. The affinity column was washed with Na3PO4 buffer (Na3PO4 50 mM pH 7.2, NaCl 0.025M, Triton X-100 0.1%), followed by triethylamine (triethylamine 20 mM pH 11, NaCl 0.25M, Triton X-100 0.1%), and Na3PO4 buffer at 1 mL/min. I was eluted with glycine 50 mM pH 3, NaCl 0.25M, Triton X-100 0.1% at 20 mL/h. SDS-PAGE showed purified I to have a mol. weight of 40,000-70,000.

=> s liposome
L11 167619 LIPOSOME

=> s l11 and diacylphosphatidylcholine
L12 68 L11 AND DIACYLPHOSPHATIDYLCHOLINE

=> s l12 and diacylphosphatidylglycerol
L13 0 L12 AND DIACYLPHOSPHATIDYLGLYCEROL

=> s l12 and molar ratio
L14 6 L12 AND MOLAR RATIO

=> dup remove l14
PROCESSING COMPLETED FOR L14
L15 2 DUP REMOVE L14 (4 DUPLICATES REMOVED)

=> d l15 1-2 cbib abs

L15 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
94163741. PubMed ID: 8118913. Influence of sphingosine on the thermal phase behaviour of neutral and acidic phospholipid liposomes. Koiv A; Mustonen P; Kinnunen P K. (Department of Medical Chemistry, University of Helsinki, Finland.) Chemistry and physics of lipids, (1993 Nov) Vol. 66, No. 1-2, pp. 123-34. Journal code: 0067206. ISSN: 0009-3084. Pub. country: Ireland. Language: English.
AB The physical state of lipids is known to have pronounced effects on membrane functions. We studied the influence of sphingosine, a modulator of diverse cellular processes on the thermal phase behaviour and molecular packing of neutral and acidic phospholipids. Differential scanning calorimetry of multilamellar liposomes as well as the monolayer technique were employed. Inclusion of sphingosine in

diacylphosphatidylcholine liposomes increased their pretransition temperature Tp until at about 10 mol% sphingosine this transition was abolished. For these liposomes a gradual increase in both the temperature Tm and enthalpy delta Hm of the main transition caused by sphingosine was observed. In contrast to diacylphosphatidylcholines, the Tp for dihexadecylphosphatidylcholine was lowered by sphingosine, demonstrating that the latter destabilizes the interdigitated gel phase. Inclusion of sphingosine in dimyristoylphosphatidic acid and dipalmitoylphosphatidylserine liposomes first elevated the Tm without significant changes in delta Hm, while at sphingosine contents > 50 mol% the appearance of complex melting profiles was evident. The transition temperature for the egg yolk phosphatidic acid was shifted from below 0 to 29 degrees C when mixed with sphingosine in a molar ratio of 1:1. Sphingosine also condensed the eggPA monolayers residing on an air-buffer interface. Accordingly, besides introducing a positive surface charge allowing the binding or activation of some proteins, sphingosine could influence membrane-mediated cellular processes by altering the organization and state of membrane lipids.

L15 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
1985:528916 Document No. 103:128916 Complex formation between di- and monophosphatidylcholines and cyclodextrins in water. Miyajima, Koichiro; Tomita, Keiko; Nakagaki, Masayuki (Fac. Pharm. Sci., Kyoto Univ., Kyoto, 606, Japan). Chemical & Pharmaceutical Bulletin, 33(6), 2587-90 (English) 1985. CODEN: CPBTAL. ISSN: 0009-2363.
AB α-, β- And γ- Cyclodextrins (CDs) interacted with phospholipid membranes causing an appreciable decrease in the surface pressure of monolayer films of dimyristoylphosphatidylcholine and a leakage of the marker, calcein [1461-15-0], in the inner aqueous phase of a liposome which was composed of diacylphosphatidylcholine (DAPC) and dicetylphosphate. The α- and γ-CDs formed white amorphous solids with DAPC in the unilamellar state in aqueous solns. The molar ratio of CD to DAPC depended on the kind of CD and the acyl chain length of DAPC. From the composition of the CD-DAPC complex, several mols. of CD included 2 acyl chains of DAPC to make complexes such as alkanoic acid-CD complexes.

=> s l11 and diacylphosphatidylglycerol
L16 8 L11 AND DIACYLPHOSPHATIDYLGLYCEROL

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17 2 DUP REMOVE L16 (6 DUPLICATES REMOVED)

=> d l17 1-2 cbib abs

L17 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
1998186612. PubMed ID: 9518643. Lateral diffusion of the total polar lipids from Thermoplasma acidophilum in multilamellar liposomes. Jarrell H C; Zukotynski K A; Sprott G D. (Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ont., Canada.) Biochimica et biophysica acta, (1998 Mar 2) Vol. 1369, No. 2, pp. 259-66. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB 31P NMR lineshapes of multilamellar liposomes composed mostly of a bilayer-spanning tetraether lipid are consistent with rapid axially symmetric motion about the bilayer normal. The residual chemical shift anisotropy of 36 ppm is comparable to that seen for diacylphosphatidylglycerol systems and suggests comparable headgroup motion. The lateral diffusion rates for Thermoplasma acidophilum total polar lipids in mutilamellar liposomes was measured by two dimensional exchange NMR as a function of temperature. At 55 degrees C, near the growth temperature, the rate of lateral diffusion,

DL, is comparable to that of diester phospholipids in the Lalpha liquid crystalline phase, having a value of 2 x 10(-8) cm2/s. DL decreases with temperature reaching a value of 8-6 x 10(-9) cm2/s at 30 degrees C. The activation energy Ea for lateral diffusion is estimated to be 10 kcal/mol (approximately 42 kJ/mol). The lateral diffusion rates indicate that the tetraether liposomes have a membrane viscosity at 30 degrees C which is considerably higher than that of diester phospholipids in the liquid crystalline phase.

L17 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2
76062453. PubMed ID: 127615. The role of phospholipid acyl chains in the activation of mitochondrial ATPase complex. Bruni A; van Dijck P W; de Gier J. Biochimica et biophysica acta, (1975 Oct 6) Vol. 406, No. 2, pp. 315-28. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB 1. The role of length and unsaturation of phospholipid acyl chains in the activation of ATPase complex was studied with synthetic phosphatidylcholines and a phospholipid-dependent preparation obtained after cholate-extraction of submitochondrial particles (Kagawa, Y. and Racker, E. (1966) J. Biol. Chemical 241, 2467--2474). 2. Micelle-forming, short-chain phosphatidylcholines produced activation only at critical micellar concentration. The reactivated complex was cold-stable but the oligomycin sensitivity was low. 3. Bilayer-forming saturated phosphatidylcholines produced activation which was maximal at 9 carbon atoms in each chain but decreased sharply as the chain-length was increased and essentially disappeared at 14 carbon atoms. By contrast the oligomycin-sensitivity increased with the increase in chain length. 4. Activation of ATPase complex reappeared when bilayers were formed with long-chain unsaturated phosphatidylcholines. The activity was oligomycin sensitive. Significant inhibition of activity was observed also after incorporation of cholesterol into the bilayers. 5. By contrast the activation induced by negatively charged liposomes of diacylphosphatidylglycerol was independent on acyl-chain composition and occurred at very low amounts of phospholipid. 6. The discontinuity in the Arrhenius plot of activity of the ATPase complex reactivated with saturated phospholipids was found at temperatures close to the gel-to-liquid crystalline transition of the lipid showing that the activity of ATPase complex was sensitive to the physical state of membrane phospholipids. 7. It is concluded that (a) reactivation of ATPase complex by isoelectric phospholipids is an interfacial activation, the minimum requirement for the lipid effect being micelle formation. (b) In order to gain the properties of the native complex a stable lamellar phase is needed. Both activity and oligomycin sensitivity are regulated by the chain length and degree of unsaturation of phospholipid acyl chains.

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=> s l11 and diacylphosphatidylethanolamine
L18          37 L11 AND DIACYLPHOSPHATIDYLETHANOLAMINE

=> dup remove l18
PROCESSING COMPLETED FOR L18
L19          21 DUP REMOVE L18 (16 DUPLICATES REMOVED)

=> s l19 and conjugate?
L20           0 L19 AND CONJUGATE?

=> s l19 and HLA
L21           0 L19 AND HLA

=> s l19 and targeting
L22           4 L19 AND TARGETING

=> dup remove l22
PROCESSING COMPLETED FOR L22
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L23 4 DUP REMOVE L22 (0 DUPLICATES REMOVED)

=> d l23 1-4 cbib abs

L23 ANSWER 1 OF 4 MEDLINE on STN

2001420819. PubMed ID: 11470091. Intermembrane transfer of polyethylene glycol-modified phosphatidylethanolamine as a means to reveal surface-associated binding ligands on liposomes. Li W M; Xue L; Mayer L D; Bally M B. (Department of Pathology and Laboratory Medicine, University of British Columbia, 2211 Wesbrook Mall, Vancouver, BC, Canada V6T 2B5.. mli@bccancer.bc.ca) . Biochimica et biophysica acta, (2001 Aug 6) Vol. 1513, No. 2, pp. 193-206. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB In order to explore the use of exchangeable poly(ethylene glycol) (PEG)-modified diacylphosphatidylethanolamines (PE) to temporarily shield binding ligands attached to the surface of liposomes, a model reaction based on inhibition and subsequent recovery of biotinylated liposome binding to streptavidin immobilized on superparamagnetic iron oxide particles (SA magnetic particles) was developed. PEG-lipid incorporation into biotinylated liposomes decreased liposome binding to SA magnetic particles in a non-linear fashion, where as little as 0.1 mol% PEG-PE resulted in a 20% decrease in binding. Using an assay based on inhibition of binding, PEG(2000)-PE transfer from donor liposomes to biotinylated acceptor liposomes could be measured. The influence of temperature and acyl chain composition on the transfer of PEG-diacyl PEs from donor liposomes to acceptor liposomes, consisting of 1,2-dioleoyl-sn-glycero-3-phosphocholine, cholesterol and N-((6-biotinoyl)amino)hexanoyl)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine (54.9:45:0.1 mole ratio), was measured. Donor liposomes were prepared using 1,2-distearoyl-sn-glycero-3-phosphocholine (50 mol%), cholesterol (45 mol%) and 5 mol% of either PEG-derivatized 1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine (DMPE-PEG(2000)), 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine (DPPE-PEG(2000)), or 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE-PEG(2000)). Transfer of DSPE-PEG(2000) to the donor liposomes was not detected under the conditions employed. In contrast, DMPE-PEG(2000) was transferred efficiently even at 4 degrees C. Using an acceptor to donor liposome ratio of 1:4, the time required for DMPE-PEG(2000) to become evenly distributed between the two liposome populations (T(EQ)) at 4 degrees C and 37 degrees C was approx. 2 and <0.5 h, respectively. An increase in acyl chain length from C14:0 to C16:0 of the PEG-lipid resulted in a significant reduction in the rate of transfer as measured by this assay. The transfer of PEG-lipid out of biotinylated liposomes was also studied in mice following intravenous administration. The relative rates of transfer for the various PEG-lipids were found to be comparable under in vivo and in vitro conditions. These results suggest that it is possible to design targeted liposomes with the targeting ligand protected while in the circulation through the use of PEG-lipids that are selected on the basis of exchange characteristics which result in exposure of the shielded ligand following localization within a target tissue.

L23 ANSWER 2 OF 4 EMBASE

2001272108 EMBASE Intermembrane transfer of polyethylene glycol-modified phosphatidylethanolamine as a means to reveal surface-associated binding ligands on liposomes. Wai Ming Li; Xue L.; Mayer L.D.; Bally M.B.. W.M. Li, Department of Pathology Medicine, University of British Columbia, 2211 Wesbrook Mall, Vancouver, BC V6T 2B5, Canada. mli@bccancer.bc.ca. Biochimica et Biophysica Acta - Biomembranes Vol. 1513, No. 2, pp. 193-206 6 Aug 2001.
Refs: 41.
ISSN: 0005-2736. CODEN: BBBMBS
S 0005-2736(01)00351-0. Pub. Country: Netherlands. Language: English.

Summary Language: English.
Entered STN: 20010823. Last Updated on STN: 20010823

AB In order to explore the use of exchangeable poly(ethylene glycol) (PEG)-modified diacylphosphatidylethanolamines (PE) to temporarily shield binding ligands attached to the surface of liposomes, a model reaction based on inhibition and subsequent recovery of biotinylated liposome binding to streptavidin immobilized on superparamagnetic iron oxide particles (SA magnetic particles) was developed. PEG-lipid incorporation into biotinylated liposomes decreased liposome binding to SA magnetic particles in a non-linear fashion, where as little as 0.1 mol% PEG-PE resulted in a 20% decrease in binding. Using an assay based on inhibition of binding, PEG(2000)-PE transfer from donor liposomes to biotinylated acceptor liposomes could be measured. The influence of temperature and acyl chain composition on the transfer of PEG-diacyl PEs from donor liposomes to acceptor liposomes, consisting of 1,2-dioleoyl-sn-glycero-3-phosphocholine, cholesterol and N-((6-biotinoyl)amino)hexanoyl)-1,2-distearoyl-sn-glycero-3- phosphoethanolamine (54.9:45:0.1 mole ratio), was measured. Donor liposomes were prepared using 1,2-distearoyl-sn-glycero-3-phosphocholine (50 mol%), cholesterol (45 mol%) and 5 mol% of either PEG-derivatized 1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine (DMPE-PEG(2000)), 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine (DPPE-PEG(2000)), or 1,2-distearoyl-sn-glycero-3-phosphoethanolamine (DSPE-PEG(2000)). Transfer of DSPE-PEG(2000) to the donor liposomes was not detected under the conditions employed. In contrast, DMPE-PEG(2000) was transferred efficiently even at 4°C. Using an acceptor to donor liposome ratio of 1:4, the time required for DMPE-PEG(2000) to become evenly distributed between the two liposome populations (T(EQ)) at 4°C and 37°C was approx. 2 and 0.5 h, respectively. An increase in acyl chain length from C14:0 to C16:0 of the PEG-lipid resulted in a significant reduction in the rate of transfer as measured by this assay. The transfer of PEG-lipid out of biotinylated liposomes was also studied in mice following intravenous administration. The relative rates of transfer for the various PEG-lipids were found to be comparable under in vivo and in vitro conditions. These results suggest that it is possible to design targeted liposomes with the targeting ligand protected while in the circulation through the use of PEG-lipids that are selected on the basis of exchange characteristics which result in exposure of the shielded ligand following localization within a target tissue.

L23 ANSWER 3 OF 4 CAPLUS
1998:435776 Document No. 129:100037 Liposomes encapsulating antiviral drugs. Bergeron, Michel G.; Desormeaux, Andre (Bergeron, Michel G., Can.). U.S. US 5773027 A 19980630, 18 pp., Cont.-in-part of U. S. Ser. No. 316,735, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-538457 19951003. PRIORITY: US 1994-316735 19941003.

AB A method is disclosed for the treatment of viral diseases comprising the administration of antiviral agents encapsulated in liposomes. Also provided are formulations of liposomes for the treatment of viral diseases and more particularly for the treatment of infections caused by viruses like human immunodeficiency virus (HIV) and cytomegalovirus (CMV). These formulations of liposomes are composed of specific classes of lipid components and contain an entrapped drug effective against the viral disease. These liposomal formulations of antiviral drugs allow high cellular penetration in different cell lines, good in vitro antiviral efficacy against HIV and CMV replication, efficient in vivo targeting of HIV reservoirs and a marked improvement of the pharmacokinetics of drugs.

L23 ANSWER 4 OF 4 CAPLUS
1996:404742 Document No. 125:67704 Liposome formulations for treatment of viral diseases. Bergeron, Michel G.; Desormeaux, Andre

(Bergeron, Michel, G., Can.). PCT Int. Appl. WO 9610399 A1 19960411, 35 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-CA561 19951003. PRIORITY: US 1994-316735 19941003.

AB A method is disclosed for the treatment of viral diseases comprising the administration of antiviral agents encapsulated in liposomes. Also provided are formulations of liposomes for the treatment of viral diseases and more particularly for the treatment of infections caused by viruses like human immunodeficiency virus (HIV) and cytomegalovirus (CMV). These formulations of liposomes are composed of specific classes of lipid components and contain an entrapped drug effective against the viral disease. These liposomal formulations of antiviral drugs allow high cellular penetration in different cell lines, good in vitro antiviral efficacy against HIV and CMV replication, efficient in vivo targeting of HIV reservoirs and a marked improvement of the pharmacokinetics of drugs.

```
=> s l11 and polyethyleneglycol
L24         692 L11 AND POLYETHYLENEGLYCOL

=> s l24 and 500 daltons
L25           0 L24 AND 500 DALTONS

=> s l24 and daltons
L26           0 L24 AND DALTONS

=> s l24 and targeting
L27         181 L24 AND TARGETING

=> s l27 and HIV
L28           4 L27 AND HIV

=> dup remove l27
PROCESSING COMPLETED FOR L27
L29          87 DUP REMOVE L27 (94 DUPLICATES REMOVED)

=> s l29 and HLA
L30           1 L29 AND HLA

=> d l30 cbib abs

L30  ANSWER 1 OF 1     MEDLINE on STN
2001048034.    PubMed ID: 11018661.   Sterically stabilized liposomes
     bearing anti-HLA-DR antibodies for targeting the
     primary cellular reservoirs of HIV-1. Bestman-Smith J; Gourde P;
     Desormeaux A; Tremblay M J; Bergeron M G. (Centre de Recherche en
     Infectiologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL,
     2705 Blvd Laurier, G1V 4G2, Quebec, QC, Canada. ) Biochimica et biophysica
     acta, (2000 Sep 29) Vol. 1468, No. 1-2, pp. 161-74.  Journal code:
     0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.
AB   The ability of liposomes bearing anti-HLA-DR Fab'
     fragments at the end termini of polyethyleneglycol chains
     (sterically stabilized immunoliposomes) to target HLA-DR
     expressing cells and increase the accumulation of liposomes into
     lymphoid organs has been evaluated and compared to that of conventional
     liposomes, sterically stabilized liposomes and
     conventional immunoliposomes after a single subcutaneous injection to
     mice.  The accumulation of sterically stabilized liposomes in
     lymph nodes was higher than that of conventional liposomes.
     Sterically stabilized immunoliposomes accumulated much better than
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conventional immunoliposomes in all tissues indicating that the presence of PEG has an important effect on the uptake of immunoliposomes by the lymphatic system. Fluorescence microscopy studies showed that sterically stabilized liposomes are mainly localized in macrophage-rich areas such as the subcapsular region of lymph nodes and in the red pulp and marginal zone of the spleen. In contrast, sterically stabilized immunoliposomes mostly accumulated in the cortex in which follicles are located and in the white pulp of the spleen. As the human HLA -DR determinant of the major histocompatibility complex class II is expressed on activated CD4+ T lymphocytes and antigen presenting cells such as monocyte/macrophages and dendritic cells, known as the cellular reservoirs of HIV-1, liposomes bearing anti-HLA-DR antibodies constitute an attractive approach to concentrate drugs in HIV-1 reservoirs and improve their therapeutic effect.

=> s l11 and "diacylphosphatidylcholine:diacylphosphatidylglycerol:diacylphosphatdylethanol-amine -polyethyleneglycol"
L31 0 L11 AND "DIACYLPHOSPHATIDYLCHOLINE:DIACYLPHOSPHATIDYLGLYCEROL:DI ACYLPHOSPHATDYLETHANOL-AMINE-POLYETHYLENEGLYCOL"

=> s l11 and dipalmitoylphoshatidylcholine
L32 8 L11 AND DIPALMITOYLPHOSHATIDYLCHOLINE

=> dup remove l32
PROCESSING COMPLETED FOR L32
L33 4 DUP REMOVE L32 (4 DUPLICATES REMOVED)

=> d l33 1-4 cbib abs

L33 ANSWER 1 OF 4 MEDLINE on STN DUPLICATE 1
2003326112. PubMed ID: 12855112. The effect of shear on the desorption of liposomes adsorbed to bacterial biofilms. Ahmed Khalid; Jones Malcolm N. (School of Biological Sciences, University of Manchester, Manchester, UK.) Journal of liposome research, (2003 May) Vol. 13, No. 2, pp. 187-97. Journal code: 9001952. ISSN: 0898-2104. Pub. country: United States. Language: English.

AB With the aid of a flow cell assembly the desorption of cationic liposomes prepared from mixtures of dipalmitoylphoshatidylcholine (DDPC), cholesterol, and either dimethyldioctadecylammonium bromide (DDAB) or 3,beta[N-(N1,N-dimethylethylenediamine)-carbamoyl]cholesterol (DC-chol) from immobilized biofilms of Staphylococcus aureus has been studied as a function of shear stress by confocal microscopy. A shear stress theory has been adapted from fluid mechanics of laminar flow between parallel plates and used to determine the critical shear stress for liposome desorption. The critical shear stress for both DDAB and DC-chol liposomes has been determined as a function of cationic lipid content and hence surface charge as reflected in their zeta potentials. The critical shear stress has been used to obtain the potential energy of liposome -biofilm interaction which together with the electrostatic interaction energy has enabled estimates of the London-Hamaker constants to be made. The values of the London-Hamaker constants at small liposome -bacterial cell separation were found to be independent of liposome composition.

L33 ANSWER 2 OF 4 EMBASE
90224950 EMBASE Document No.: 1990224950. Gastric protective activity of mixtures of saturated polar and neutral lipids in rats. Lichtenberger L.M.; Romero J.J.; Kao Y.-C.J.; Dial E.J.. Dept. Physiology/Cell Biology, University of Texas, Medical School, P.O. Box 20708,Houston, TX 77225, United States. Gastroenterology Vol. 99, No. 2, pp. 311-326 1990. ISSN: 0016-5085. CODEN: GASTAB

Pub. Country: United States. Language: English. Summary Language: English. Entered STN: 911213. Last Updated on STN: 911213

AB It has been shown that intragastric treatment of rats with a suspension of dipalmitoylphoshatidylcholine and tripalmitin at a 1:4 ratio (5 mg lipid/mL per rat) provided rats with highly efficaceous and consistent protection against a variety of ulcerogenic agents and conditions. The gastric protective activity of this mixture was of long duration (t(1/2) .apprx. 9 hours). In an attempt to understand the mechanism of protection, it was determined that the ulcerogen-induced reduction in gastric surface hydrophobicity was reversed in rats pretreated with the mixture. However, the lipid mixture did not affect the gastric emptying rate and maintained its cytoprotective activity in indomethacin-treated rats. These results indicate that the mixture's protective effect was not mediated by alterations in either gastrointestinal motility or the gastric accumulation of lipids or 'cytoprotective' metabolites (prostaglandins). The mixture also appreciably reduced gastric lesion score in response to acid if one or both the lipids was substituted for a metabolically inert ether analogue, suggesting that lipid metabolism makes a negligible contribution to the protective response. Electron microscopic observation indicated that the predominant structure in the mixture is a microemulsion in which a dipalmitoylphosphatidylcholine monolayer encapsulates a tripalmitin core. Last, the improved gastric protective activity of the mixture in comparison to dipalmitoylphosphatidylcholine liposomes is discussed regarding marked differences in the physical structure of the two suspensions and the rate at which lipids in these states adsorb to a surface to enhance its hydrophobic properties.

L33 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

1987:529485 Document No. 107:129485 The influence of calcium on the turbidity of DPPC-DMPA vesicles within the temperature range of the phase transition. Cools, Ardouin A.; Janssen, Lambert H. M. (Dep. Pharm. Chem., State Univ. Utrecht, Utrecht, 3511 GH, Neth.). Physiological Chemistry and Physics and Medical NMR, 18(3), 171-9 (English) 1986. CODEN: PCPNER. ISSN: 0748-6642.

AB The influence of Ca2+ on the phase behavior of liposomes composed of dipalmitoylphosphatidylcholine (DPPC) and dimyristoylphosphatidic acid (DMPA) in a ratio of 4:1 was investigated by turbidity measurements. In the absence of Ca2+ a single phase transition at 42° was observed for the mixed phospholipids. Following addition of Ca2+, scans through the temperature range of this phase transition appeared to favor fusion of the vesicles. However when Ca2+ was added to the vesicles isothermally, 2 sep. phase transitions were observed These 2 transitions were at temps. approximating the phase transition temps. of DMPA and DPPC individually in the absence of Ca2+, i.e., 39 and 43°, resp.

L33 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

1985:483799 Document No. 103:83799 On the phase diagram of an L-dipalmitoylphosphatidylcholine/cholesterol mixture. Koinova, R.; Boyanov, A.; Tenchov, B. (Cent. Lab. Biophys., Bulg. Acad. Sci., Sofia, 1113, Bulg.). FEBS Letters, 187(1), 65-8 (English) 1985. CODEN: FEBLAL. ISSN: 0014-5793.

AB The effects of cholesterol (I) on the subtransition, pretransition, and main transition of L-dipalmitoylphosphatidylcholine (II) liposomes were determined by DSC, and possible explanations for these effects are discussed. Among these explanations is a immiscibility loop in the I-II phase diagram.

=> s l11 and distearolphosphatidylcholine
L34 1 L11 AND DISTEAROLPHOSPHATIDYLCHOLINE

=> d l34 cbib abs

L34 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN

1987:472593 Document No. 107:72593 Partition of malathion in synthetic and

native membranes. Antunes-Madeira, M. C.; Madeira, Vitor M. C. (Dep. Zool., Cent. Biol. Cel., Coimbra, Port.). Biochimica et Biophysica Acta, Biomembranes, 901(1), 61-6 (English) 1987. CODEN: BBBMBS. ISSN: 0005-2736.

AB Partition coeffs. of [14C]malathion in model and native membranes are affected by temperature, cholesterol content, and lipid chain length. Partition in egg phosphatidylcholine bilayers decreases linearly with temperature, over a range (10-40°) at which the lipid is in the liquid-crystalline state. Addition of 50 mol% cholesterol severely decreases partition and partially abolishes the temperature dependence. First-order phase transitions of dimyristoyl-, dipalmitoyl- and distearolphosphatidylcholines (DMPC, DPPC, and DSPC) are accompanied by a sharp increase in malathion partition. Apparently, the insecticide is easily accommodated in bilayers of short-aliphatic-chain lipids, since the partitions were 225, 135 and 48 in DMPC, DPPC and DSPC, resp., at temps. 10 degrees below the midpoint of their transitions. Partition values in native membranes decrease sequentially as follows: sarcoplasmic reticulum, mitochondria, brain microsomes, myelin and erythrocytes. This dependence parallels the relative content of cholesterol and is similar in liposomes of total extracted lipids, although the absolute partitions showed decreased values.

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=> s l11 and dipalmitoylphosphatidylglycerol
L35         768 L11 AND DIPALMITOYLPHOSPHATIDYLGLYCEROL

=> s l35 and DPPC
L36         228 L35 AND DPPC

=> s l36 and "10:3"
L37           0 L36 AND "10:3"

=> s l36 and targeting
L38          19 L36 AND TARGETING

=> s l38 and HLA
L39           0 L38 AND HLA

=> s l38 and HIV
L40           0 L38 AND HIV

=> dup remove l38
PROCESSING COMPLETED FOR L38
L41            6 DUP REMOVE L38 (13 DUPLICATES REMOVED)

=> d l41 1-6 cbib abs
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L41 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

2006:1157476 Document No. 145:477896 Liposomes comprising phospholipid-conjugated vector compounds. Cuthbertson, Alan (GE Healthcare A/S, Norway). PCT Int. Appl. WO 2006115416 A2 20061102, 26pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-NO157 20060425. PRIORITY: NO 2005-1995 20050425.

AB The present invention relates to a process for the manufacture of targeting liposomes comprising vector compds. conjugated to the hydrophilic part of modified phospholipids. The present invention

provides a modified phospholipid for use as membrane material for liposomes and also a modified phospholipid binding a targeting vector. Liposomes can carry a paramagnetic metal at the surface making the liposomes useful as diagnostic contrast agent for use in MRI. Thus, liposomes were prepared containing DPPC, DPPG, and 4-formylbenzenamido-PEG3400-DSPE (preparation given) with a weight ratio of lipids at 90:5:5, resp., by the thin film hydration method., and subsequently conjugated with an aminooxy-modified peptide.

L41 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 1
1998184997. PubMed ID: 9524311. The interaction of phospholipid liposomes with bacteria and their use in the delivery of bactericides. Jones M N; Song Y H; Kaszuba M; Reboiras M D. (School of Biological Sciences, University of Manchester, U.K.) Journal of drug targeting, (1997) Vol. 5, No. 1, pp. 25-34. Journal code: 9312476. ISSN: 1061-186X. Pub. country: Switzerland. Language: English.
AB Liposomes have been prepared from dipalmitoylphosphatidylcholine (DPPC) incorporating the cationic lipids stearylamine (SA), dimethyldioctadecylammonium bromide (DDAB) and dimethylaminoethane carbamoyl cholesterol (DCchol) and the anionic lipids dipalmitoylphosphatidylglycerol (DPPG) and phosphatidylinositol (PI). Their adsorption to biofilms of skin-associated bacteria (Staphylococcus epidermidis and Proteus vulgaris) and oral bacteria (Streptococcus mutans and sanguis) has been investigated as a function of mole % cationic and anionic lipid. Targeting (adsorption) was most effective for the systems DPPC-chol-SA, DPPC-DPPG and DPPC-PI liposomes to S. epidermidis. The effect of extracellular mucopolysaccharide on targeting was investigated for S. epidermidis biofilms. It was found that targeting increased with the level of extracellular mucopolysaccharide for all liposome compositions studied. The delivery of the oil-soluble bactericide Triclosan and the water soluble bactericide chlorhexidine was studied for a number of liposomal compositions. Superior delivery of both bactericides relative to the free bactericide occurred for DPPC-chol-SA liposomes and for Triclosan delivery by DPPC-DPPG and DPPC-PI liposomes targeted to S. epidermidis at low bactericide concentrations. DPPC-chol-SA liposomes were also effective for delivery of Triclosan to S. sanguis biofilms. Double labelling experiments using [14C]-chlorhexidine and [3H]-DPPC suggested that there was exchange between adsorbed liposomes which had delivered bactericide to the biofilm and those in the bulk solution implying a diffusion mechanism for bactericide delivery.

L41 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2
96392063. PubMed ID: 8798875. Tumor targeting in vivo by means of thermolabile fusogenic liposomes. Zellmer S; Cevc G. (Technische Universitat Munchen, Medizinische Biophysik, Klinikum r.d.I., Germany.) Journal of drug targeting, (1996) Vol. 4, No. 1, pp. 19-29. Journal code: 9312476. ISSN: 1061-186X. Pub. country: Switzerland. Language: English.
AB Thermolabile fusogenic liposomes were devised based on the stoichiometric 1/2 mixtures of dipalmitoylphosphatidylcholine (DPPC) and elaidic acid (ELA) and from the similar stoichiometric mixtures of DPPC, dipalmitoylphosphatidylglycerol (DPPG) and elaidoyl alcohol (EL-OH) or palmitelaidoyl alcohol (PEL-OH). The resulting vesicle suspensions are fusogenic in the region of hyperthermia (> or = 42 degrees C) and can be targeted selectively to the heated tumor tissue. Incorporation of DPPG or fatty alcohols into the vesicle membranes also leads to a non-specific, temporary vesicle material accumulation in the lung, however, probably due to platelet activation. Vesicle material accumulation in A-431 tumors, xenotransplanted in nude mice, after 30 min of local hyperthermia (42 degrees C) is 4-fold higher for the DPPC/ELA (1/2), 2.8-fold higher for the DPPC

/DPPG/EL-OH (0.8/0.2/2) and 3.7-fold higher for the DPPC /ELA/EL-OH (1/1/1) mixtures than for similar vesicles used at the physiological temperature. Extension of hyperthermia to 60 min induces a 7.8-fold relative material accumulation in the tumor tissue when the thermolabile, fusogenic DPPC/ELA/EL-OH (1/1/1) vesicles are used. Simple DPPC vesicles only reach concentrations in the heated tumor or muscle tissue that are 1.85-fold and 1.38-fold higher than in the normothermic control, respectively. This is probably a consequence of simple vasodilatation. In vitro experiments revealed that the adsorption of serum proteins to the vesicle membrane decreases the chain-melting phase transition temperature and the transition enthalpy of vesicle suspension. Adsorption is most prominent at the chain-melting phase transition temperature of the mixed lipid bilayers, which is also the critical temperature for the induction of liposome fusion. This hampers the practical use of the resulting vesicle suspension in vivo. The serum-induced decrease of the chain-melting phase transition temperature, which is likely to change as a function of time in vivo, depends on the lipid composition and on the local surface charge density of vesicles. Incorporation of ELA and DPPG concentrations above 15 mol-%, for example, reduce the extent of protein adsorption onto vesicles. This has to be borne in mind when devising vesicles for practical applications.

L41 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 3

94327253. PubMed ID: 8050822. Therapeutic effect of adriamycin encapsulated in long-circulating liposomes on Meth-A-sarcoma-bearing mice. Oku N; Doi K; Namba Y; Okada S. (Department of Radiobiochemistry, School of Pharmaceutical Sciences, University of Shizuoka, Japan.) International journal of cancer. Journal international du cancer, (1994 Aug 1) Vol. 58, No. 3, pp. 415-9. Journal code: 0042124. ISSN: 0020-7136. Pub. country: United States. Language: English.

AB Long-circulating liposomes modified with a uronic-acid derivative, palmityl-D-glucuronide (PGlcUA), have been developed previously for the passive targeting of liposomes to tumor tissues. In this study, we examined the therapeutic effect of adriamycin (ADM) encapsulated in PGlcUA liposomes composed of dipalmitoylphosphatidylcholine (DPPC), cholesterol (Chol) and PGlcUA (molar ratio, 40/40/10) since this amount of PGlcUA was enough to endow liposomes with long-circulating activity. Long-circulating activity was also observed with palmityl-D-galacturonide (PGalUA) modified liposomes, suggesting that uronic acid plays an important role in preventing liposomes from being trapped in the reticuloendothelial system (RES). ADM was loaded in liposomes by a remote-loading method. Free or liposomal ADM was injected i.v. into BALB/c mice bearing s.c.-implanted Meth-A sarcoma. The liposomal formulation was efficient for reducing tumors, prolonging survival time and curing the animals, especially in the case of large tumors where free ADM was not. Furthermore, PGlcUA liposomes were more effective than conventional liposomes containing dipalmitoylphosphatidylglycerol (DPPG) instead of PGlcUA for prolonging survival time in mice. It might therefore be appropriate to use PGlcUA liposomes as the carriers of anticancer drugs.

L41 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 4

95078251. PubMed ID: 7986811. The targeting of phospholipid liposomes to bacteria. Jones M N; Kaszuba M; Reboiras M D; Lyle I G; Hill K J; Song Y H; Wilmot S W; Creeth J E. (School of Biological Sciences, University of Manchester, UK.) Biochimica et biophysica acta, (1994 Nov 23) Vol. 1196, No. 1, pp. 57-64. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Phospholipid liposomes have been prepared from phospholipid mixtures including dipalmitoylphosphatidylcholine/phosphatidylinositol (DPPC/PI) and DPPC/dipalmitoylphosphatidylglycerol** * (***DPPC/DPPG) mixtures and targeted to adsorbed biofilms of the skin-associated bacteria Staphylococcus epidermidis and Proteus vulgaris and the oral bacterium Streptococcus sanguis. The effects of

time, liposome concentration and density of bacteria in the biofilm have been studied in detail for Staphylococcus epidermidis. The targeting (as assessed by the apparent monolayer coverage of the biofilms by liposomes) to the biofilms was found to be sensitive to the mol% of PI and DPPG in the liposomes and optimum levels of PI were found for targeting to each bacterium. The use of PI and DPPG-containing liposomes for the delivery of the bactericide, Triclosan, to biofilms of Staphylococcus epidermidis was studied as a function of the amount of Triclosan carried by the liposomes. All the liposome systems tested inhibited the growth of bacteria from the biofilms after brief (2 min) exposure to Triclosan-carrying liposomes. At low Triclosan levels bacterial growth inhibition by Triclosan-carrying liposomes exceeded that by an equivalent level of free Triclosan. After short periods (min) of exposure of biofilms to Triclosan-carrying liposomes the bactericide was shown to preferentially concentrate in the biofilms relative to its liposomal lipid carrier. The results suggest that phospholipid liposomes with appropriately chosen lipid composition have potential for the targeting and delivery of bactericide to bacteria.

L41 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
1987:454705 Document No. 107:54705 Thermodynamic characterization of interactions between ornithine transcarbamylase leader peptide and phospholipid bilayer membranes. Myers, Melanie; Mayorga, Obdulio L.; Emtage, Jennifer; Freire, Ernesto (Dep. Biol., Johns Hopkins Univ., Baltimore, MD, 21218, USA). Biochemistry, 26(14), 4309-15 (English) 1987. CODEN: BICHAW. ISSN: 0006-2960.

AB The interactions of the targeting sequence of mitochondrial ornithine transcarbamylase with phospholipid bilayers of different mol. compns. were studied by high-sensitivity heating and cooling DSC, high-sensitivity isothermal titration calorimetry, fluoroscence spectroscopy, and electron microscopy. These studies indicated that the leader peptide interaction strongly with dipalmitoylphosphatidylcholine (DPPC) bilayer membranes containing small mole percents of the anionic phospholipids, dipalmitoylphosphatidylglycerol (DPPG) or brain phosphatidylserine (brain PS), but not with pure phosphatidylcholines. For the 1st time, the energetics of the leader peptide-membrane interaction were measured directly by using calorimetric techniques. At 20°, the association of the peptide with the membrane was exothermic and characterized by an association constant of 2.3 + 106 M-1 in the case of phosphatidylglycerol-containing and 0.35 + 106 M-1 in the case of phosphatidylserine-containing phospholipid bilayers. In both cases, the enthalpy of association was -60 kcal/mol of peptide. Addnl. expts. using fluorescence techniques suggested that the peptide did not penetrate deeply into the hydrophobic core of the membrane. The addition of the leader peptide to DPPC /DPPG (5:1) or DPPC/brain PS (5:1) small sonicated vesicles resulted in vesicle fusion. The fusion process was dependent on peptide concentration and was maximal at the phase transition temperature of the vesicles and minimal at temps. below the phase transition.

=> s (bergeron m?/au or desormeaux a?/au or tremblay m?/au)
L42 4994 (BERGERON M?/AU OR DESORMEAUX A?/AU OR TREMBLAY M?/AU)

=> s l42 and lipsome
L43 0 L42 AND LIPSOME

=> s l42 and liposome
L44 105 L42 AND LIPOSOME

=> s l44 and HLA
L45 26 L44 AND HLA

=> dup remove l45
PROCESSING COMPLETED FOR L45
L46 7 DUP REMOVE L45 (19 DUPLICATES REMOVED)

=> d l46 1-7 cbib abs

L46 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2005:427376 Document No.: PREV200510225950. Lymphoid tissue targeting of anti-HIV drugs using liposomes. Desormeaux, Andre; Bergeron, Michel G.. CHU Quebec, Ctr Rech Infectiol, RC 709,Pavillon CHUI, Quebec City, PQ G1V 4G2, Canada. Duzgunes, N [Editor]. (2005) pp. 330-351. Methods in Enzymology. Publisher: ELSEVIER ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495 USA. Series: METHODS IN ENZYMOLOGY.
ISSN: 0076-6879 (print). ISBN: 0-12-182796-8(H). Language: English.
AB Considering that HIV-1 accumulates and replicates actively within lymphoid tissues, any strategy that will decrease viral stores in these tissues might be beneficial to the infected host. Follicular dendritic cells (FDC), B lymphocytes, antigen-presenting cells like macrophages, and activated CD4(+) T cells are abundant in lymphoid tissues, and all express substantial levels of the HLA-DR determinant of the major histocompatibility complex class II (MHC-II). Monocyte-derived macrophages, which are also CD4(+) and express HLA-DR, are considered to be the most frequent hosts of HIV-I in tissues of infected individuals. This chapter describes a method for the generation of sterically stabilized immunoliposomes grafted with anti-HLA-DR antibodies that allows efficient delivery of drugs to lymphoid tissues. The method first involves the production of murine HLA-DR (clone Y-17, IgG(2b)) and human HLA-DR (clone 2.06, IgG(1)) antibodies from hybridomas in mice and their purification from ascites fluids. This step is followed by the production of Fab' fragments of antibodies 2.06 and Y-17 that are grafted at the surface of sterically stabilized immunoliposomes instead of the complete IgG to reduce their immunogenicity. The preparation of sterically stabilized liposomes, the composition of which allows an efficient entrapment and retention of several drugs, by the method of thin lipid film hydratation followed by extrusion through polycarbonate membranes is then described. This step is followed by the removal of unencapsulated drug, when present, by low-speed centrifugation of the liposomal preparation through a Sephadex G-50 column. These liposomes contain a fixed amount of poly(ethylene glycol) chain terminated by a maleimide reactive group for the coupling of Fab' fragments. The procedure for the coupling of Fab' fragments at the surface of sterically stabilized liposomes and the removal of uncoupled fragments of antibodies is described. In vitro binding studies of sterically stabilized immunoliposomes to cell lines expressing different surface levels of the mouse or human HLA-DR determinant of MHC-II demonstrate that these liposomes are very specific. When compared with conventional liposomes, the subcutaneous administration in the upper back, below the neck, of mice of anti-HLA-DR immunoliposomes resulted in a 2.9 and 1.6 times greater accumulation in the cervical and brachial lymph nodes, respectively. The use of sterically stabilized immunoliposomes increases 2 to 4.6 times the concentration of liposomes in all tissues, with a peak accumulation at 240 h in brachial, inguinal, and popliteal lymph nodes and at 360 h or greater in cervical lymph nodes. A single bolus injection of indinavir given subcutaneously to mice results in no significant drug levels in lymphoid organs. Most of the injected drug accumulates in the liver and,is totally cleared within 24 h postadministration. In contrast, sterically stabilized immunoliposomes are very efficient in delivering high concentrations of indinavir to lymphoid tissues for at least 15 days postinjection. The drug accumulation in all tissues leads to a 21- to 126-fold increased accumulation when compared with the free agent. Anti-HLA-DR immunoliposomes containing indinavir are as efficient as the free agent in inhibiting HIV-1 replication in PM1 cells that express

high levels of cell surface HLA-DR.Sterically stabilized anti-HLA-DR immunoliposomes mostly accumulate in the cortex in which follicles (B cells and FDCs) are located, and in parafollicular areas in wich T cells, interdigitating dendritic cells, and other accessory cells are abundant. The delivery of drugs in this area of the lymph nodes could represent a convenient strategy to inhibit more efficiently HIV-1 replication. Although the method described in this chapter is specific to the coupling of anti-HLA-DR antibodies, any antibody fragment or peptide specific for an antigen present in relatively large quantities at the surface of lymphoid cells, that is anchored to the surface of sterically stabilized liposomes with an appropriate coupling method, can be used to concentrate drugs within target tissues and improve the therapeutic effect of drugs.

L46 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 1

2005092527. PubMed ID: 15721390. Lymphoid tissue targeting of anti-HIV drugs using liposomes. Desormeaux Andre; Bergeron Michel G. (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Quebec, Canada.) Methods in enzymology, (2005) Vol. 391, pp. 330-51. Journal code: 0212271. ISSN: 0076-6879. Pub. country: United States. Language: English.

AB Considering that HIV-1 accumulates and replicates actively within lymphoid tissues, any strategy that will decrease viral stores in these tissues might be beneficial to the infected host. Follicular dendritic cells (FDC), B lymphocytes, antigen-presenting cells like macrophages, and activated CD4(+) T cells are abundant in lymphoid tissues, and all express substantial levels of the HLA-DR determinant of the major histocompatibility complex class II (MHC-II). Monocyte-derived macrophages, which are also CD4(+) and express HLA-DR, are considered to be the most frequent hosts of HIV-1 in tissues of infected individuals. This chapter describes a method for the generation of sterically stabilized immunoliposomes grafted with anti-HLA-DR antibodies that allows efficient delivery of drugs to lymphoid tissues. The method first involves the production of murine HLA-DR (clone Y-17, IgG(2b)) and human HLA-DR (clone 2.06, IgG(1)) antibodies from hybridomas in mice and their purification from ascites fluids. This step is followed by the production of Fab' fragments of antibodies 2.06 and Y-17 that are grafted at the surface of sterically stabilized immunoliposomes instead of the complete IgG to reduce their immunogenicity. The preparation of sterically stabilized liposomes, the composition of which allows an efficient entrapment and retention of several drugs, by the method of thin lipid film hydratation followed by extrusion through polycarbonate membranes is then described. This step is followed by the removal of unencapsulated drug, when present, by low-speed centrifugation of the liposomal preparation through a Sephadex G-50 column. These liposomes contain a fixed amount of poly(ethylene glycol) chain terminated by a maleimide reactive group for the coupling of Fab' fragments. The procedure for the coupling of Fab' fragments at the surface of sterically stabilized liposomes and the removal of uncoupled fragments of antibodies is described. In vitro binding studies of sterically stabilized immunoliposomes to cell lines expressing different surface levels of the mouse or human HLA-DR determinant of MHC-II demonstrate that these liposomes are very specific. When compared with conventional liposomes, the subcutaneous administration in the upper back, below the neck, of mice of anti-HLA-DR immunoliposomes resulted in a 2.9 and 1.6 times greater accumulation in the cervical and brachial lymph nodes, respectively. The use of sterically stabilized immunoliposomes increases 2 to 4.6 times the concentration of liposomes in all tissues, with a peak accumulation at 240 h in brachial, inguinal, and popliteal lymph nodes and at 360 h or greater in cervical lymph nodes. A single bolus injection of indinavir given subcutaneously to mice results in no significant drug levels in lymphoid organs. Most of the injected drug accumulates in the liver and is totally cleared within 24 h postadministration. In contrast,

sterically stabilized immunoliposomes are very efficient in delivering high concentrations of indinavir to lymphoid tissues for at least 15 days postinjection. The drug accumulation in all tissues leads to a 21- to 126-fold increased accumulation when compared with the free agent. Anti-HLA-DR immunoliposomes containing indinavir are as efficient as the free agent in inhibiting HIV-1 replication in PM1 cells that express high levels of cell surface HLA-DR. Sterically stabilized anti-HLA-DR immunoliposomes mostly accumulate in the cortex in which follicles (B cells and FDCs) are located, and in parafollicular areas in which T cells, interdigitating dendritic cells, and other accessory cells are abundant. The delivery of drugs in this area of the lymph nodes could represent a convenient strategy to inhibit more efficiently HIV-1 replication. Although the method described in this chapter is specific to the coupling of anti-HLA-DR antibodies, any antibody fragment or peptide specific for an antigen present in relatively large quantities at the surface of lymphoid cells, that is anchored to the surface of sterically stabilized liposomes with an appropriate coupling method, can be used to concentrate drugs within target tissues and improve the therapeutic effect of drugs.

L46 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2

2002053847. PubMed ID: 11779569. Targeted delivery of indinavir to HIV-1 primary reservoirs with immunoliposomes. Gagne Jean-Francois; Desormeaux Andre; Perron Sylvie; Tremblay Michel J; Bergeron Michel G. (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, 2705 Blvd Laurier, Universite Laval, Quebec, QC, Canada.) Biochimica et biophysica acta, (2002 Feb 1) Vol. 1558, No. 2, pp. 198-210. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The tissue distribution of indinavir, free or incorporated into sterically stabilized anti-HLA-DR immunoliposomes, has been evaluated after a single subcutaneous injection to C3H mice. Administration of free indinavir resulted in low drug levels in lymphoid organs. In contrast, sterically stabilized anti-HLA-DR immunoliposomes were very efficient in delivering high concentrations of indinavir to lymphoid tissues for at least 15 days post-injection increasing by up to 126 times the drug accumulation in lymph nodes. The efficacy of free and immunoliposomal indinavir has been evaluated in vitro. Results showed that immunoliposomal indinavir was as efficient as the free agent to inhibit HIV-1 replication in cultured cells. The toxicity and immunogenicity of repeated administrations of liposomal formulations have also been investigated in rodents. No significant differences in the levels of hepatic enzymes of mice treated with free or liposomal indinavir were observed when compared to baseline and control untreated mice. Furthermore, histopathological studies revealed no significant damage to liver and spleen when compared to the control group. Liposomes bearing Fab' fragments were 2.3-fold less immunogenic than liposomes bearing the entire IgG. Incorporation of antiviral agents into sterically stabilized immunoliposomes could represent a novel therapeutic strategy to target specifically HIV reservoirs and treat more efficiently this retroviral infection.

L46 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

2000:790356 Document No. 133:340273 Methods and formulations for targeting infectious agents bearing host cell proteins. Bergeron, Michel G. ; Desormeaux, Andre; Tremblay, Michel J. (Infectio Recherche Inc., Can.). PCT Int. Appl. WO 2000066173 A2 20001109, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA469 20000503.

PRIORITY: CA 1999-2270600 19990503.

AB A formulation is disclosed for the treatment of diseases caused by an infectious agent which acquires host membranes protein during its life cycle. The formulation is a targeting pharmaceutical composition It comprises a ligand capable of binding the host membrane proteins coupled to a lipid-comprising vesicle, which may comprise or not a drug effective in the treatment of the disease. Specific liposomes bearing anti-HLA-DR or anti-CD4 antibodies comprising or not antiviral drugs, namely anti-HIV drugs, are disclosed and claimed. A method of formulation as well as a method of using the formulation in the treatment of a disease are also disclosed.

L46 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 3

2001338262. PubMed ID: 11101055. Targeting cell-free HIV and virally-infected cells with anti-HLA-DR immunoliposomes containing amphotericin B. Bestman-Smith J; Desormeaux A; Tremblay M J; Bergeron M G. (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Canada.) AIDS (London, England), (2000 Nov 10) Vol. 14, No. 16, pp. 2457-65. Journal code: 8710219. ISSN: 0269-9370. Pub. country: ENGLAND: United Kingdom. Language: English.

AB OBJECTIVE: To evaluate the ability of liposomes bearing anti-HLA-DR Fab' fragments (immunoliposomes) and containing amphotericin B (AmB) to target and neutralize cell-free HIV-1 particles and virally-infected cells. METHODS: The effect of AmB on the attachment and fusion of HIV-1(NL4-3) to Jurkat E6.1 cells has been evaluated using a p24 enzymatic assay. The ability of AmB to inhibit HIV-1-based luciferase reporter viruses pseudotyped with HXB2, AML-V and VSV-G envelopes has been evaluated in Jurkat E6.1 cells. The efficacy of free and immunoliposomal AmB to inhibit cell-free HIV, that have incorporated or not HLA -DR molecules, has been evaluated in HLA-DR/negative (NEG) 1G5 T cells and HLA-DR/positive (POS) Mono Mac 1 cells. RESULTS: AmB inhibited HIV infectivity independently of the nature of viral envelope proteins. Pretreatment of HIV with AmB had no major effect on viral attachment and fusion process to Jurkat E6.1 cells. Immunoliposomal AmB (0.5 microg/ml) led to a 77% inhibition of replication of HLA -DR/POS HIV-1 with no cell toxicity, whereas free AmB had no significant antiviral activity at this concentration. A complete inhibition of viral replication was observed following incubation of viruses with immunoliposomal AmB (2.5 microg/ml). Anti-HLA-DR immunoliposomes containing AmB had no effect on the infectivity of HLA-DR/NEG HIV-1 particles in HLA-DR/NEG T lymphoid cells but completely inhibited replication of viruses in an HLA -DR/POS monocytic cell line. CONCLUSION: The incorporation of neutralizing agents in anti-HLA-DR immunoliposomes could represent a novel therapeutic strategy to specifically target cell-free HIV particles and virally-infected cells to treat HIV infection more efficiently.

L46 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 4

2001048034. PubMed ID: 11018661. Sterically stabilized liposomes bearing anti-HLA-DR antibodies for targeting the primary cellular reservoirs of HIV-1. Bestman-Smith J; Gourde P; Desormeaux A; Tremblay M J; Bergeron M G. (Centre de Recherche en Infectiologie, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, 2705 Blvd Laurier, G1V 4G2, Quebec, QC, Canada.) Biochimica et biophysica acta, (2000 Sep 29) Vol. 1468, No. 1-2, pp. 161-74. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments at the end termini of polyethyleneglycol chains (sterically stabilized immunoliposomes) to target HLA-DR expressing cells and increase the accumulation of liposomes into lymphoid organs has been evaluated and compared to that of conventional liposomes , sterically stabilized liposomes and conventional

immunoliposomes after a single subcutaneous injection to mice. The accumulation of sterically stabilized liposomes in lymph nodes was higher than that of conventional liposomes. Sterically stabilized immunoliposomes accumulated much better than conventional immunoliposomes in all tissues indicating that the presence of PEG has an important effect on the uptake of immunoliposomes by the lymphatic system. Fluorescence microscopy studies showed that sterically stabilized liposomes are mainly localized in macrophage-rich areas such as the subcapsular region of lymph nodes and in the red pulp and marginal zone of the spleen. In contrast, sterically stabilized immunoliposomes mostly accumulated in the cortex in which follicles are located and in the white pulp of the spleen. As the human HLA-DR determinant of the major histocompatibility complex class II is expressed on activated CD4+ T lymphocytes and antigen presenting cells such as monocyte/macrophages and dendritic cells, known as the cellular reservoirs of HIV-1, liposomes bearing anti-HLA-DR antibodies constitute an attractive approach to concentrate drugs in HIV-1 reservoirs and improve their therapeutic effect.

L46 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 5
2000001973. PubMed ID: 10518698. Targeting lymph nodes with liposomes bearing anti-HLA-DR Fab' fragments. Dufresne I; Desormeaux A; Bestman-Smith J; Gourde P; Tremblay M J ; Bergeron M G. (Centre de Recherche en Infectiologie, Universite Laval, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, 2705 Blvd. Laurier, Quebec, QC, Canada.) Biochimica et biophysica acta, (1999 Oct 15) Vol. 1421, No. 2, pp. 284-94. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The ability of liposomes bearing anti-HLA-DR Fab' fragments to target cells expressing the human HLA-DR determinant of the major histocompatibility complex class II (MHC-II) has been evaluated and compared to that of conventional liposomes. Anti-HLA-DR immunoliposomes did not bind to HLA -DR-negative cells. In contrast, a high level of binding was observed following incubation of immunoliposomes with cells bearing important levels of human HLA-DR. The accumulation of conventional and murine anti-HLA-DR immunoliposomes in different tissues has been investigated following a single subcutaneous injection given in the upper back of C3H mice. Anti-HLA-DR immunoliposomes resulted in a much better accumulation in the cervical and brachial lymph nodes when compared to conventional liposomes. The accumulation in the liver was similar for both liposomal preparations, whereas an approximately twofold decrease in accumulation was observed for immunoliposomes in the spleen. Given that HLA-DR surface marker is expressed on monocyte/macrophages and activated CD4+ T lymphocytes, the primary cellular reservoirs of the human immunodeficiency virus (HIV), the use of liposomes bearing surface-attached anti-HLA-DR could constitute a convenient strategy to more efficiently treat this debilitating retroviral disease. Moreover, the reported incorporation of high amounts of host-encoded HLA-DR proteins by HIV particles renders the use of liposomes bearing anti-HLA-DR antibodies even more attractive.

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FULL ESTIMATED COST	222.53	222.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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